

AMENDMENTS TO THE CLAIMS

1-25. (Previously canceled)

26. (Amended) A sustained release formulation comprising of an aqueous soluble biopolymer, wherein the formulation is one or more biologically active molecules prepared by a process comprising exposure of the biologically active molecules biopolymer in aqueous solution to an organic solvent under conditions resulting in a precipitate which releases the biopolymer in a sustained release fashion in aqueous solution, lyophilate or crystal.

27. (Amended) The formulation of claim 26, wherein the biopolymer and a carrier protein in the aqueous solution are exposed to the organic solvent biologically active molecules are released from the formulation for a period of at least 24 hours.

28. (Previously Added) The formulation of claim 26 or 27, wherein the biopolymer is released from the formulation for a period is of at least 48 24 hours.

29. (Canceled) The formulation of claim 27, wherein the period is at least 7 days.

30. (Canceled) A sustained release formulation comprising a precipitate, lyophilate or crystals of a polypeptide prepared by exposure of the polypeptide in aqueous solution to an organic solvent, which polypeptide is released from the formulation in aqueous solution over a period of at least 24 hours.

31. (Amended) The formulation of claim 30 28, wherein the period is at least 48 hours.

32. (Amended) The formulation of claim 30 28, wherein the period is at least 7 days.

33. (Amended) The A sustained release formulation of claim 26 or 27, comprising a precipitate, lyophilate or crystals of a biologically active polypeptide prepared by a process comprising exposure of the polypeptide in aqueous solution to wherein the organic solvent is a polar protic organic solvent, and the which formulation, when administered to a patient, releases said biopolymer polypeptide at a rate which provides an average steady state concentration of at least the ED₅₀ for the biopolymer polypeptide for a period of at least 2 days.

34. (Previously Added) The formulation of claim 33, wherein the period is at least 7 days.

35. (Previously Added) The formulation of claim 33, wherein the period is at least 14 days.

36. (Previously Added) The formulation of claim 33, wherein the period is at least 21 days.
37. (Previously Added) The formulation of claim 33, wherein the period is at least 50 days.
38. (Previously Added) The formulation of claim 33, wherein the period is at least 100 days.
39. (Amended) The formulation of any of claims 26, 30 or 27 and 33, wherein the organic solvent is an alcohol, an aldehyde, a ketone, a hydrocarbon, an aromatic hydrocarbon, or a mixture thereof.
40. (Amended) The formulation of any of claims 26, 30 or 27 and 33, wherein the organic solvent is an alcohol or mix of alcohols.
41. (Previously Added) The formulation of claim 39, wherein the alcohol is a lower alcohol, or mixture thereof.
42. (Previously Added) The formulation of claim 39, wherein the alcohol is selected from the group consisting of methanol, ethanol, isopropanol, n-propanol, n-butanol, isobutanol, and t-butanol, or a mixture thereof.
43. (Amended) The formulation of claim 26 or 27 30, wherein the organic solvent is a polar protic solvent.
44. (Amended) The formulation of claim 26 or 30 43, wherein the organic solvent is a water-miscible polar protic solvent.
45. (Previously Added) The formulation of claim 33, wherein the organic polar protic solvent is water-miscible.
46. (Amended) The formulation of any of claims 26, 30 or 27 and 33, wherein the ~~biologically active molecules or polypeptides are biopolymer~~ is released from the formulation in vivo at a rate which provides an average steady state concentration of at least the ED₅₀ for the biologically active molecules or polypeptides for a period of at least 2 days.
47. (Previously Added) The formulation of claim 46, wherein the period is at least 7 days.
48. (Previously Added) The formulation of claim 46, wherein the period is at least 14 days.
49. (Previously Added) The formulation of claim 46, wherein the period is at least 21 days.
50. (Previously Added) The formulation of claim 46, wherein the period is at least 50 days.
51. (Previously Added) The formulation of claim 46, wherein the period is at least 100 days.

52. (Amended) The formulation of ~~any of~~ claims 26, 30 or 27 and 33, wherein the organic solvent(s) are chosen such that, when administered to a patient, the solvent is released from the formulation at a rate which provides an average steady state concentration which remains at least one order of magnitude below the IC₅₀ for deleterious side effects, if any, of the solvent.
53. (Amended) The formulation of claim 26 or 27, wherein ~~the biopolymer logically active molecule is a polymer is~~ selected from the group consisting of a peptide, a nucleic acid, an oligonucleotide, a carbohydrate, a ganglioside, or a glycan.
54. (Amended) The formulation of claim 26 or 27, wherein ~~the biopolymer logically active molecule~~ is a polypeptide.
55. (Amended) The formulation of claim 30, 33 or 54, wherein the polypeptide is selected from the group consisting of cytokines, growth factors, somatotropin, growth hormones, colony stimulating factors, erythropoietin, plasminogen activators, enzymes, T-cell receptors, surface membrane proteins, lipoproteins, clotting factors, anticoagulants, tumor necrosis factors, transport proteins, homing receptors, and addressins.
56. (Amended) The formulation of claim 30, 33 or 54, wherein the polypeptide is selected from the group consisting of rennin; human growth hormone; bovine growth hormone; growth hormone releasing factor; parathyroid hormone; thyroid stimulating hormone; lipoproteins; α -1-antitrypsin; insulin; proinsulin; follicle stimulating hormone; calcitonin; luteinizing hormone; glucagon; a clotting factor such as factor VIIIC, factor IX, tissue factor, and von Willebrand's factor; anti-clotting factors; atrial natriuretic factor; lung surfactant; a plasminogen activator; bombesin; thrombin; hemopoietic growth factor; tumor necrosis factor- α ; tumor necrosis factor- β ; enkephalinase; RANTES (regulated on activation normally T-cell expressed and secreted); human macrophage inflammatory protein (MIP-1- α); a serum albumin; müllerian-inhibiting substance; relaxin A-chain; relaxin B-chain; prorelaxin; gonadotropin-associated peptide; a microbial protein; DNase; inhibin; activin; vascular endothelial growth factor (VEGF); receptors for hormones or growth factors; integrin; protein A; protein D; rheumatoid factors; a neurotrophic factor; platelet-derived growth factor (PDGF); a fibroblast growth factor; epidermal growth factor (EGF); transforming growth factors (TGF); insulin-like growth factor-I; insulin-like growth factor-II; des(1-3)-IGF-I (brain IGF-I); insulin-like growth factor binding proteins; CD proteins; erythropoietin; osteoinductive factors; immunotoxins; an interferon; colony stimulating factors (CSFs); interleukins (ILs); superoxide dismutase; T-cell receptors; surface membrane proteins; decay accelerating

factor; antigens; transport proteins; homing receptors; addressins; regulatory proteins; immunoglobulin-like proteins; antibodies; and nucleases, or fragments thereof.

57. (Amended) The formulation of claim 26 or 27, wherein ~~biopolymerlogically active molecule~~ is selected from the group consisting of a lipid and a sterol.

58. (Amended) The formulation of claim 26 or 27, wherein the ~~biopolymerlogically active molecule~~ is a small an organic compound.

59. (Canceled) The formulation of ~~any of~~ claims 26, 30 and 33, which is a precipitate.

60. (Canceled) The formulation of ~~any of~~ claims 26, 30 and 33, which is a lyophilate.

61. (Canceled) A formulation comprising a lyophilate of a polypeptide, which lyophilate is formed from a solution by a process comprising exposure of the polypeptide in aqueous solution to a polar protic organic solvent, and has a solubility rate in a bodily fluid over a period of at least 24 hours that is at least 2 fold less than a lyophilate of the polypeptide from aqueous solution.

62. (Canceled) The formulation of claim 61, wherein the period is at least 48 hours.

63. (Canceled) The formulation of claim 61, wherein the period is at least 168 hours.

64. (Canceled) The formulation of claim 61, wherein the solubility rate is at least 10 fold less than a lyophilate of the polypeptide formed from aqueous solutions.

65. (Canceled) The formulation of claim 61, wherein the solubility rate is at least 25 fold less than a lyophilate of the polypeptide formed from aqueous solutions.

66. (Canceled) The formulation of claim 61, wherein the bodily fluid is serum.

67. (Amended) A medicament for administration to an animal, comprising the formulation of ~~any of~~ claims 26, 30 or 27 and 33.

68. (Previously Added) The medicament of claim 67, for administration to a mammal.

69. (Previously Added) The medicament of claim 67, for administration to a human.

70. (Amended) A method for manufacturing a medicament comprising formulating the formulation of ~~any of~~ claims 26, 30 or 27 and 33 with a pharmaceutically acceptable excipient.

71. (Canceled) A method for manufacturing a slow release formulation of a biologically active molecule, comprising (a) exposing said biologically active molecules to an organic solvent, and (b) forming a precipitate, lyophilate or crystal.

72. (Canceled) ~~Use of a sustained release formulation of any of claims 26, 30 and 33, in the manufacture of a pharmaceutical preparation in single dosage form.~~
73. (New) The formulation of claim 54, wherein the polypeptide is an interferon.